

LEAD EXPOSURE AND TELOMERE LENGTH IN ELDERLY MEN: THE NORMATIVE AGING STUDY

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Background and Aims: Telomeres, repeated DNA sequences at the ends of chromosomes, are important for genomic stability. Telomere shortening has emerged as a marker of cellular aging and increased risk of early mortality. Recently, exposure to traffic pollution has been associated with shortened telomeres.

This study examined the associations between measures of lead exposure and telomere length in a cohort of aging men.

Methods: In the Veteran's Affairs Normative Aging Study, cumulative baseline lead exposure was measured by K-Shell X-Ray Fluorescence microscopy of tibia and patella bones between 1991-2002 ($n_{\text{subjects}} = 589$) and acute blood lead exposure by GFAAS ($n_{\text{subjects}} = 701$). Telomere length was determined at up to four repeated study visits between 1999-2007 ($n_{\text{visits}} = 1183$) by the ratio of telomere sequence repeat to single copy gene (T/S ratio) from real time PCR of whole blood DNA. The first visit cross-sectional effect of lead and other exposures on log(T/S ratio) was determined by generalized additive modeling. Mixed models with repeated telomere measurements and fixed effects of lead were also generated. Potential confounders included smoking, alcohol ingestion and metabolic parameters.

Results: Median telomere T/S ratio at the first visit (aged 55-100) was 1.22 (IQR: 0.503) and at the fourth visit was 1.07 (IQR: 0.712). Lead exposure measured by tibia, patella, and blood lead had no relationship with telomeres cross-sectionally, but was associated with longer telomeres in repeated measures mixed effects models. Telomere measures were inversely associated with age ($p\text{-value} < 0.0001$), current smoking status, ischemic heart disease status and body mass index. Higher attained education was associated with longer telomeres.

Conclusions: Telomere length shortens in elderly men with age. The degree of shortening is influenced by smoking status, body mass index, education level, and ischemic heart disease diagnosis. In contrast to previous research on traffic exposure and telomere length, lead exposure was associated with longer telomeres. Possible explanations will be discussed.